PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 490267 SMR/paq	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International Application No. **PCT/NZ2003/000232**	International Filing Date *(day/month/year)* 20 October 2003	Priority Date *(day/month/year)* 18 October 2002

International Patent Classification (IPC) or national classification and IPC

Int. Cl.[7] A61K 38/01, 38/17, 6/00; A61P 19/08, 1/00

Applicant

SILCOCK, Patrick Joseph et al

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheet(s).

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand 4 May 2004	Date of completion of the report 24 February 2005
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer **G.J. McNEICE** Telephone No. (02) 6283 2055

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/NZ2003/000232

I. Basis of the report

1. With regard to the **elements** of the international application:*

[X] the international application as originally filed.

[ ] the description, pages , as originally filed,
pages , filed with the demand,
pages , received on with the letter of

[ ] the claims, pages , as originally filed,
pages , as amended (together with any statement) under Article 19,
pages , filed with the demand,
pages , received on with the letter of

[ ] the drawings, pages , as originally filed,
pages , filed with the demand,
pages , received on with the letter of

[ ] the sequence listing part of the description:
pages , as originally filed
pages , filed with the demand
pages , received on with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4. [ ] The amendments have resulted in the cancellation of:

[ ] the description, pages

[ ] the claims, Nos.

[ ] the drawings, sheets/fig.

5. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 44-51	YES
	Claims 1-43	NO
Inventive step (IS)	Claims 44-51	YES
	Claims 1-43	NO
Industrial applicability (IA)	Claims 1-51	YES
	Claims	NO

2. Citations and explanations (Rule 70.7)

D1. O'Sullivan, M.M. "Influence of transglutaminase treatment on some physico-chemical properties of milk" Journal of Dairy Research (2002) 69, pages 433-442 (accepted for publication 20 March 2002)

D2. Aboumahmoud, R. et al "Crosslinking of Whey Protein by Transglutaminase" J. Dairy Science (1990) 73, p256-263. See pages 257 & 259

D3. Aoki, T. et al "Caseins are cross-linked through their ester phosphate groups by colloidal calcium phosphate" Biochimica et Biophysica Acta (1987) 911, pages 238-243

D4. Zhang, Z. P. "Behaviour of Calcium and Phosphate in Artificial Casein Micelles" J. Dairy Science (1996) 79, pages 1722-1727

D5. Aoki, T. "The Least Number of Phosphate Groups for Crosslinking of Casein by Colloidal Calcium Phosphate" J. Dairy Science (1992) 75: pages 971-975. See especially pages 971 and 974.

Novelty (N): Claims 1- 51

An hydrolysate of casein is a breakdown product which occurs when casein, a protein found in milk, is broken down by enzymes or acids.

D1 discloses, at page 436, below the figure, milk which is cold renneted to hydrolyse κ-casein followed by addition of Transglutaminase (TGase) to cross-link the casein. At page 438, milk has plasmin added to it to extensively cross-link the β-casein and partially hydrolyse the α_{s1}-casein before partially cross-linking with TGase. Claims 1-38, 42 and 43 are therefore not novel.

Milk is well known to include strontium and fluoride. In relation to Strontium in milk, see, e.g. "Strontium", Retrieved from the internet:<URL:http://www.nei.org/documents/USNRCStrontium.pdf> which states
Stable strontium is the 15th most abundant element in nature and it is the most abundant trace element in seawater. Thus, it can become incorporated into all plants and animal tissues. ...The daily intake of strontium varies from about 1.8 to 2.0 mg/day. Of this ... approximately 60 to 90 percent by food.... Strontium is present naturally in many foods .
Intake. ... Milk and milk-byproducts are the major contributors of Sr-90 in western countries. .

In relation to fluoride in milk, see. e.g. R.W. Kahama et al, The Effect of Intrinsic Fluoride in Cows' Milk on in vitro Enamel Demineralization, Caries Research 1998; 32: p200-203 [Retrieved from the internet: <URL:http://content.karger.com/ProdukteDB/produkte.asp?Doi=16453#AC>]
The fluoride concentration in cows' milk has been reported to vary with the fluoride levels in drinking water but it seldom exceeds 0.5 µg/ml ... ... The 36% reduction in calcium loss at pH 5.0 by treatment with milk with only 0.3 µg/ml fluoride is an indication that intrinsic milk fluoride has some caries-protective properties.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box V

Milk is therefore known to be a source of strontium and fluoride and, being a common food, is suitable as a mouthwash. Claims 39 to 41 are therefore also not novel.

D2 to D5 disclose crosslinking of casein, but not of an hydrolysate of casein. Claims 1-43 are therefore novel in relation to D2 to D5.

The citations do not disclose or fairly suggest remineralising or treating or preventing dental caries, tooth erosion , dental hypersensitivity or gingivitis (claim 44), nor preparations where the hydrolysis is of 3-8% of the peptide bonds (claims 45-51). Therefore claims 44-51 are novel and involve an inventive step.

Inventive Step (IS): Claims 1-51

As for Novelty

Industrial Applicability (IA): Claims 1-51

Compositions for bioactive metal ion delivery, phosphoprotein preparations and treatments for dental conditions are industrially applicable.